

REMARKS

Applicants note that all amendments of Claims presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),¹ and without waiving the right to prosecute the amended Claims (or similar Claims) in the future.

In the Final Office Action dated November 13, 2008, the Examiner objected to Claims 22 and 23 as being dependent upon a base claim, but allowable if rewritten in independent form. The Applicants have rewritten Claims 22 and 23 as new independent Claim 26. As such, the Applicants submit that the objection is moot.

In the Final Office Action dated November 13, 2008, the Examiner rejected Claims 18-21 and 24-25 under 35 U.S.C. 103(a) as allegedly being obvious in light of Erisir et al. (J. Neurophysiology, 1999, 82:2476; hereinafter Erisir), Baranauskas et al. (J. Neuroscience 1999, 10:6394; hereinafter Baranauskas), Tkatch et al (Society for Neuroscience, 1999, 25L Abstract 179.17), Weiser et al. (J. Neuroscience, 15:4298 (1995); hereinafter Weiser), Tuschl et al (WO 02/44321; hereinafter Tuschl), and Low et al. (U.S. Patent 6,071,891; hereinafter Low).

The Applicants respectfully disagree with the rejection. Nonetheless, in order to further the business interests of the Applicants, and without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the cancelled claims (or similar claims) in the future, the Applicants have amended Claim 18 to recite that the inhibition of Kv3.4 expression results in a decrease in said sustained high frequency discharge in cells comprising the Kv complex but not in cells lacking said co-assembled complex. None of the cited references, alone or in combination, teach such an element of the claims.

In response to the Applicants' prior arguments, the Examiner states "Based on Baranauskas et al., GP are considered fast spiking neurons and therefore it was known in the art that fast spiking neurons were known to express Kv3.4 channels as compared to non fast spiking neurons. Further, Tkatch et al. recognized the normal high frequency burst produced by GP neurons was increased in Parkinson's disease patients and noticed this increase in bursting is due

¹ 65 Fed. Reg. 54603 (Sept. 8, 2000).

to the broadening of action potentials and suggested the Kv3.4 channels may be responsible for such broadening.” (Office Action, pg. 4). The Applicants respectfully disagree with the rejection and submit that the Examiner has failed to fully consider the Applicants’ prior arguments. The Applicants will not re-iterate their prior arguments but instead direct the Examiner to arguments already in the record.²

The Examiner further states “There is no subjective evidence e.g. a reference, presented with the declaration filed on 08/06/2008 to substantiate the opinion of Dr. Surmeier that Kv3.4 subunits were not important to the ability of neurons to spike at high frequencies when in fact there were important.” (Office Action, pg. 6). The Applicants respectfully disagree. For example, the Erisir et al. reference cited by the Examiner in the present rejection states that the fast-spiking and rapid repolarization of the action potential was fully explained by the properties of Kv3.1-2 subunits (See e.g., abstract).

The Applicants further provide the second declaration of Dr. Surmeier. Dr. Surmeier’s second declaration states that additional references explain the fast spiking properties of neurons without the inclusion of Kv3.4 include (Macica et al., 2001 and Macica et al. 2003; both of which are attached hereto). Dr. Surmeier’s declaration further states that in 2003, there were no publications arguing that Kv3.4 subunits were important in spike repolarization in neurons; most of the interest in Kv3.4 subunits was focused on muscle, based upon the statement in the Weiser et al., reference included in the present rejection that the predominant expression of this channel was in muscle, not in the brain.

Dr. Surmeier’s declaration explains that, in addition to their predominant location in muscle, the role of Kv3.4 subunits in modulating the properties of Kv3 channels in neurons had been dismissed for two reasons. First, based on previously published work (Weiser et al and Rudy et al. (attached hereto)), Kv3.4 channels were thought to inactivate rapidly, making it impossible for them to contribute to spike repolarization during high frequency repetitive discharge (as found in globus pallidus neurons). Heteromeric channels containing Kv3.4 and Kv3.1 subunits also were thought to rapidly inactivate (see Rudy et al). Experiments conducted during the course of development of embodiments of the present invention showed that heteromeric channels containing a novel splice variant of Kv3.4 subunit (Kv3.4c) do not inactivate rapidly as previously shown for the Kv3.4b splice variant.

Dr. Surmeier’s declaration further states that based upon published work (Weiser et al, Rudy et al.), Kv3.4 containing channels were not capable of opening soon enough in an action

² See applicants response to Office Action mailed 2/6/08.

potential to contribute in a significant way to spike repolarization. Experiments conducted during the course of development of embodiments of the present invention and published (Baranauskas et al.; attached hereto) showed that this is only true of the Kv3.4b splice variant of Kv3.4 but not of the Kv3.4c splice variant that dominates channels in globus pallidus neurons. This splice variant shifts the voltage-dependence of Kv3.4 gating by 10-15 mV, allowing Kv3.4 containing channels to open soon after the beginning of a spike. This was an unexpected and important finding, meriting its publication in Nature Neuroscience, one of the premier neuroscience journals in the world.

Thus, the Applicants submit that they have provided evidence, both external and in the form of Dr. Surmeier's second declaration, to support the statement that the results described in the present application were unexpected and contrary to the current state of the art and the time of filing of the present application.

Thus, the Applicants submit that the Examiner has not demonstrated a prima facie case of obvious because the cited references do not teach all of the elements of the present invention. In addition, even if the Examiner has demonstrated a prima facie case of obviousness,³ the Applicants have provided rebuttal evidence in the form of unexpected results. As such, the Applicants submit that the Claims are not obvious and respectfully request that the rejection be withdrawn.

CONCLUSION

It is respectfully submitted that the invention as claimed fully meets all requirements and that the claims are worthy of allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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³ The Applicants submit that the Examiner has not demonstrated a prima facie case of obviousness.